EXHIBIT D

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ORIGINAL ARTICLE

Tensile properties of five commonly used mid-urethral slings relative to the TVT™

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Abstract We characterized the tensile properties of five mid-urethral slings relative to the Gynecare TVT™. Slings were divided and loaded to failure. The heat-sealed Boston Scientific mid-section and the American Medical Systems (AMS) tensioning suture were examined separately. Analysis of the resulting nonlinear load elongation curves included calculation of low and high stiffness, the transition point between them (inflection point), load at failure, and relative elongation. Permanent elongation was measured after repetitive loads. Mean values were compared using a one-way analysis of variance. The curves of the Gynecare, Boston Scientific (no midsection) and AMS (no suture) were nonlinear with similar low stiffness and inflection points. The Bard, Caldera, and Mentor slings were stiffer. Heat sealing the Boston Scientific mid-section increased stiffness, while the AMS suture had negligible effect. Cyclical loading induced permanent elongation that was similar for Gynecare, AMS, and Boston Scientific (without mid-section) and lower for Bard, Caldera, and Mentor. With the exception of AMS, the overall effect of newer sling modifications was an increase in tensile stiffness.

Keywords Stress urinary incontinence · Mid-urethral slings · Polypropylene mesh · Cyclical loading · Permanent elongation

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Introduction

The "tension-free" vaginal tape (TVT™) originally described by Ulmsten et al. [1] is a mid-urethral sling comprised of a synthetic wide-pore polypropylene mesh (Gynecare division of Ethicon, Somerville, NJ, USA). The sling is relatively uniform in composition throughout its length with tanged edges designed to "grip" tissue after sling placement. Long-term follow-up has shown very good objective cure rates in prospective observational studies [2, 3], similar cure rates to the Burch colposuspension in a prospective randomized trial [4], and overall low rates of postoperative voiding dysfunction [5, 6]. As a result of its success and relative ease of use, the minimally invasive mid-urethral sling has been widely adopted throughout the world in the surgical treatment of stress urinary incontinence.

Although the TVT was the first mid-urethral sling to gain widespread acceptance, numerous other mid-urethral sling systems have subsequently been introduced. While all of the meshes consist of a knitted polypropylene material, they have been altered as a marketing strategy to overcome clinician-perceived deficiencies in the TVT. For example,

one of the primary problems in using the TVT is that as a result of its low stiffness, the mesh easily deforms when tensioning under the urethra. Specifically, pulling the sling gently results in thinning of the mesh (permanent deformation) and fraying at the tanged edges. Consequently, various companies have modified polypropylene sling meshes for easier placement by heat sealing the mid-portion of the sling that lays under the urethra (Boston Scientific, Natick, MA, USA) or placing a patented "tensioning suture" along the longitudinal axis (American Medical Systems, Minnetonka, MN, USA). Others have changed the knitting pattern completely (Bard, Covington, GA, USA; Caldera, Agoura Hills, CA, USA; and Mentor, Santa Barbara, CA, USA) and decreased the pore size (Caldera and Mentor) so that the sling is more resistant to deformation when handled. Although the modifications have simplified the technical aspects of sling placement, it is not clear how these changes affect the biomechanical behavior of the sling and, ultimately, clinical outcomes. Indeed, to date, most outcome data fail to distinguish between different types of sling meshes most likely because the basic biomechanical properties of most sling products have not been defined [7].

In addition to outcomes, biomechanical properties of sling material may contribute to sling complications. Specific known postoperative complications associated with mid-urethral slings include voiding dysfunction (de novo urinary urgency and urge incontinence, and incomplete bladder emptying), erosion of the mesh into the urethra or bladder, vaginal exposure of mesh, and fistula formation [8–10]. The quality of the host tissue and the technique of sling placement also contribute to these complications; however, these factors are well known to most surgeons. It is knowledge of the properties of the sling material that surgeons have the greatest knowledge deficit and consequently are completely dependent on the mesh information supplied by a representative of the vendor. Even more problematic is that many of the representatives have little knowledge of biomechanical factors that may be relevant and tend to focus on aspects of the sling which facilitate the operation for the surgeon. This practice may not be the best approach and may impact clinical outcomes. Instead, before implanting a sling, the operating surgeon should have a basic working knowledge of the biomechanical properties and behavior of the material he or she is using. These data would provide the clinician with a better knowledge of which slings may be comparable in the clinical setting as well as an ability to communicate with bioengineers specific features of slings that were desirable. In addition, a common language between clinicians and bioengineers of common biomechanical behaviors shared by different manufacturer's slings may improve clinical outcomes by allowing slings with similar or distinct properties to be studied in clinical trials. Moreover, it may improve recognition of adverse outcomes that may be attributable to a specific mesh property (e.g., stiffness).

In the following study, we therefore, aimed to perform an in-depth analysis in which the biomechanical properties of six commonly used polypropylene mid-urethral slings were tested. To do this, we performed a uniaxial load to failure test and cyclical loading tests. We were primarily interested in comparing the relative resistance of the slings to deformation (stiffness), the degree to which the slings deformed after the application of a load (relative elongation), the load at which the slings failed (ultimate load at failure), and their overall biomechanical behavior. For simplicity of data presentation, we used the Gynecare TVT™ as the gold standard and defined the behavior of five newer versions of the mid-urethral sling relative to it.

Materials and methods

Preparation of the meshes

Six commonly used mid-urethral polypropylene slings were obtained: Gynecare TVT™/TVT-O™ (n=5), American Medical Systems SPARC/Monarc™ (AMS; N=5), Mentor Aris™ (N=5), Boston Scientific Advantage/Obtryx™ (N=5), Bard Uretex™ (N=5), and Caldera T-sling™ (N=5, Table 1). Each sling was carefully removed from its packaging and laid flat. The polypropylene mesh portion of each sling was isolated from the surgical hardware, and the plastic casing that protects the meshes was removed (Aris™ is not packaged with a protective sleeve). Subsequently, a 0.5-cm segment was removed from the end of each sling for imaging. Three to four samples measuring 7–8 cm in length were then cut from the remaining mesh in the Gynecare, AMS, Mentor, Bard, and Caldera slings. This length was chosen, as it roughly approximates the length of sling that is implanted in patients. For the AMS sling, the tensioning suture was removed for separate testing before sling division. For the Boston Scientific sling, the heat-sealed midsection (~4.5 cm in length) with non-tanged edges was separated from the remainder of the tanged-edged mesh (~20.5 cm on either side of the mid-portion). Samples from the tanged portion were cut into 7- to 8-cm segments, while the entire heat sealed section was tested separately (N=5).

Tensile testing protocol

Eight samples from each group (samples obtained from five different slings), and five Boston Scientific midsections were utilized for a tensile test to failure. A custom-made clamp with triangulated teeth was used to secure the ends (1.5 cm) of each sample. The edge of the last tooth was

Table 1 Textile properties (including load at failure) provided by the manufacturers listed at the top (AMS, American Medical Systems) describing the different meshes tested in this study

Mesh type	Gynecare	Boston Scientific	AMS	Bard	Caldera	Mentor
Mesh thickness	0.63 mm	0.66 mm	0.66 mm	0.62 mm	0.48 mm	0.27 mm
Pore size	1379 μm	1182 μm	1000 μm	1160 μm	698 μm	374 μm
Fiber size (diameter)	0.15 mm	0.15 mm	0.15 mm	0.13 mm	0.15 mm	0.08 mm
Weight (g/m^2)	100	100	110	81	140	70
Relative porosity	53.9%	57.7%	52.1%	N/A	68.2%	N/A
Load at failure	70 N	70 N	65.6 N	60 N	70 N	76 N
Mesh edges/features	Tanged	Tanged/heat sealed midsection	Tanged/tensioning suture	Tanged	Not tanged	Not tanged; sealed edges

filed to minimize stress concentrations which would cause premature failure during testing. For consistency, the samples each had an aspect ratio (length between the clamps divided by the sample width) of approximately eight. This ensured that during testing, samples were loaded with uniform stress distribution, thus, allowing for comparable results between slings. Only the midsection of the Boston Scientific sling had a smaller aspect ratio measuring 3–3.5. Clamp to clamp distances were measured using calipers which were accurate to within 0.02 mm.

After preparation, each clamp-sample-clamp construct was placed into a 37°C saline bath which was rigidly attached to the base of an Instron™ 5565 screw-driven mechanical testing machine (Fig. 1). The inferior clamp was fixed to the bottom of the saline bath, while the superior clamp was fixed through a load cell (50 lb or 225 N model 31 Sensotec™ transducer) to the crosshead of the testing machine (Fig. 1). The load cell had a resolution of 0.01 N with an accuracy of 0.05 N. Once fixed to the testing machine, each sample was allowed to equilibrate in a slack position for 5 min before testing. For tensile testing, samples were preloaded to 0.1 N to remove any slack within the sample, and the elongation of the testing machine was set to zero. The samples were then loaded to failure at an elongation rate of 50 mm/min. The data collected from the testing machine included the load measured by the load cell in Newtons and the elongation of the specimen which corresponds to the displacement of the crosshead measured in millimeters (mm).

An additional four to five samples per group obtained from three different slings (N=3 for Boston Scientific midsection only samples) were subjected to a three-step cyclic loading protocol (C1–C3) to determine how samples permanently elongate under repetitive loading. It should be noted that the permanent elongation of these samples is mostly due to a rearranging of the sling's architecture and should not be confused with the traditional mechanics definition of plastic deformation of an elastic material. We based our testing on the assumption that under most circumstances, the slings would be subjected to brief consecutive loads as a result of daily activities that would not result in failure of the mesh. For this protocol, samples

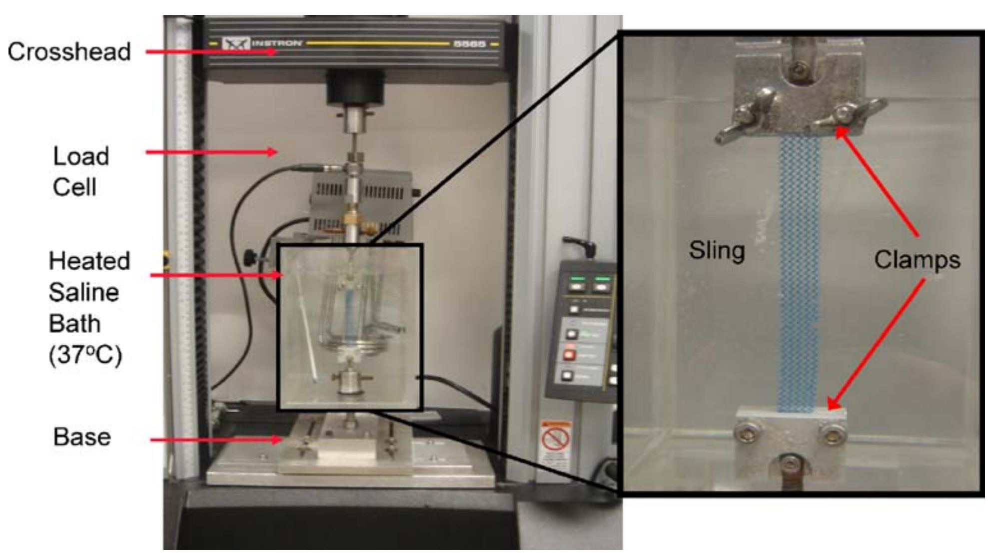

Fig. 1 The tensile testing setup demonstrating a Gynecare™ sample mounted to a materials testing machine. As shown in the magnified inset, the sample is emerged in a saline bath and is rigidly fixed with customized clamps. The upper clamp is contiguous with a load cell that is connected to the crosshead of the machine

were again preloaded to 0.1 N to remove any slack within the sample, and the elongation of the testing machine was set to zero. For the first step of the cyclic loading protocol (C1), samples were cycled between 0.5 to 5 N for ten cycles (C1). After the completion of C1, samples were again preloaded to 0.1 N to remove any slack, and the change in crosshead displacement from the initial preload (measured in mm) was recorded. For the second step of the cyclic loading protocol (C2), samples were cycled between 0.5 and 15 N for ten cycles. The upper force limit was chosen, as it lies in the upper range of loads applied to slings in vivo[5]. After the completion of C2, samples were again preloaded to 0.1 N to remove any slack, and change in crosshead displacement from the initial preload (measured in mm) was recorded. For the third step of the cyclic loading protocol (C3), the protocol from C1 was repeated and a preload to 0.1 N was again applied. The change in crosshead displacement from the initial preload was recorded.

To account for differences in initial length of samples from different companies, the measured elongation was divided by the initial clamp to clamp distance to calculate the relative elongation of each sample. Thus, load vs relative elongation (%) curves were plotted and utilized to determine parameters describing the tensile properties of each sample. The load to failure curves generally displayed bilinear behavior with an initial low stiffness linear region followed by a high stiffness linear region. Thus, the initial low slope was defined as the minimum slope over a 15% interval of relative elongation. The high stiffness was defined as the maximum slope over a 30% interval of relative elongation. The intercept of two tangent lines fit in these regions was defined as the inflection point and used to represent a transition point in stiffness. The load and relative elongation at the point of failure were also recorded. For the cyclic loading protocol, the relative change in elongation at each step was recorded as a measure of the amount of permanent elongation in response to cyclic loading.

Statistical analysis

For sample size calculation, we based our analysis on the initial data obtained from testing four Gynecare TVT™ slings. Accordingly, we estimated that five samples per group were needed to detect a minimum of a 100% difference in low stiffness, 15% difference in inflection, and 75% difference in permanent elongation between Gynecare and other brands with a power of 80%.

For statistical analysis, a one-way analysis of variance was used to evaluate differences between samples from each company. Pairwise post hoc comparisons were made between Gynecare and the other brands using Dunnett's multiple comparisons procedure. The significance level was 0.05.

Results

The textile properties provided by the companies are shown in Table 1. From these, it is apparent that with the exception of the heat-sealed midsection of Boston Scientific and the tensioning suture of the AMS slings, the Gynecare, Boston Scientific and AMS meshes are very similar. The Bard mesh was similar to this group, with the exception that it weighed less and failed at a lower load. Mentor was distinct with a small pore and fiber size and smooth edges, while the properties of the Caldera sling were somewhat intermediate. Interestingly, the mechanical parameter most often reported by the companies, load at failure (tensile strength), suggested that overall, mechanically, all of the slings were very similar. However, according to our testing, this was not the case (see below). The macroscopic images demonstrating the knit patterns of each mesh are shown in Fig. 2. The images showed a similar pattern among the Gynecare, Boston Scientific, and AMS meshes. The Caldera, Bard, and Mentor meshes had distinct knit patterns. As suggested by the textile properties provided

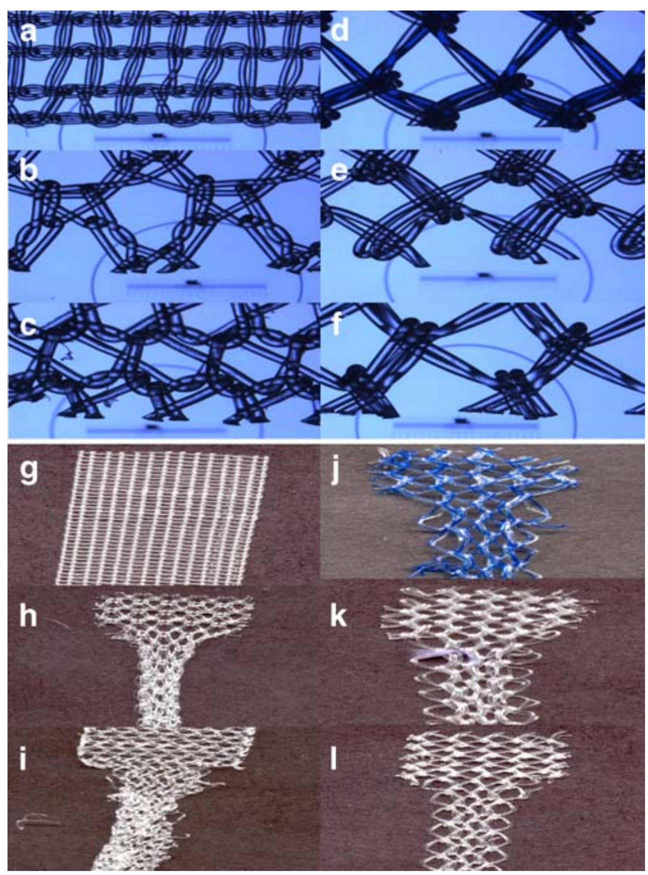

Fig. 2 Macroscopic images of samples from Mentor (**a** and **g**), Bard (**b** and **h**), Caldera (**c** and **i**), Gynecare (**d** and **j**), AMS (**e** and **k**, tensioning suture along longitudinal axis not shown), and Boston Scientific slings (**f** and **l**, heat sealed midsection not shown) before (**a** **f**) and after (**g** **l**) and applied load

by the companies, Mentor had the tightest knit pattern (smallest pore size) followed by Caldera and then Bard. The edges of the Mentor and the heat-sealed midsection of the Boston Scientific slings (not shown) are smooth. A comparison of the slings in the clamped portion (non-loaded) and the loaded portion immediately before failure (Fig. 2g–l) demonstrates that the behavior of the Mentor sling is distinct with minimal elongation even at high loads.

In Table 2, the tensile properties of each sling are reported relative to those of the Gynecare TVT™. The Boston Scientific and AMS slings were tested separately from the heat-sealed midsection and the tensioning suture, respectively. The results of mechanical testing demonstrate that the general shape of the load vs relative elongation curves obtained from the load to failure tests of the Gynecare, Boston Scientific (without the mid-section), AMS, and Bard samples were nonlinear, with an initial region of low stiffness followed by a transition to a region of high stiffness (Fig. 3a). The low stiffness region (Table 2) showed similar values for Gynecare, the tanged portion of the Boston Scientific, Bard, and AMS with values of 0.09±0.01, 0.05±0.03, 0.16±0.07, and 0.09±0.03 N/mm, respectively ($p>0.05$). The midsection of the Boston Scientific samples was stiffer, with a low stiffness value that was six times larger (0.58±0.15 N/mm, $p<0.001$). In contrast, the load to failure curves of the Mentor and Caldera slings were completely dissimilar to the others. First, the load elongation curves generated by them were linear, displaying a uniform stiffness throughout the test. These slings were also substantially stiffer, with a linear stiffness measuring 1.5±0.04 and 1.2±0.3, respectively (Fig. 3b). Thus, for the first 60% of elongation, these samples were 17 times stiffer than the Gynecare TVT™ (Table 2, $p<0.001$). Because the curves of the Mentor and Caldera slings were linear, only a single stiffness value is shown in Table 2.

The inflection point, or transition to the high stiffness region (Fig. 3a and Table 2), was similar between samples from Gynecare, AMS, and the tanged portion of the Boston Scientific ranging from relative elongations of 66.4±6.1% (AMS) to 71.2±2.5% (Gynecare). These points corresponded with loads of approximately 10 N or 2.25 lbs. The inflection points of the Bard samples and midsections of the Boston Scientific slings, on the other hand, were significantly lower, occurring at 38.3±9.5 and 20.1±3.4% relative elongation, respectively ($p<0.05$). The midsection of the Boston Scientific sling demonstrated the lowest inflection point of these samples indicating overall increased stiffness ($p<0.05$). For both Bard and the midsection of the Boston Scientific sling, these inflection points corresponded to a load between 5 and 10 N.

For the high stiffness region, it is noteworthy that at this point in the testing protocol, the mesh architecture was completely altered (Fig. 2g–l, Fig. 4). Indeed, with the exception of the stiffer Mentor and Caldera slings, the

Table 2 Parameters obtained from the load elongation curves generated after a uniaxial load to failure test on the six meshes listed in the leftmost column

Mesh	Low stiffness (N/mm)	High stiffness (N/mm)	Relative elongation at inflection point (%)	Load at failure (N)	Relative elongation at failure (%)
Gynecare	0.09±0.01[a]	2.0±0.3	71.2±2.5	73.5±11.8	108.1±4.5
Bost Sci[b]	0.05±0.03	1.9±0.1	68.8±5.5	69.6±8.3	107.3±10.0
AMS	0.09±0.03	1.7±0.2	66.4±6.1	79.2±5.5	115.2±7.4
Bard	0.16±0.07	1.2±0.1	38.3±9.5	59.8±5.1	92.3±6.7
Caldera	1.2±0.3	N/A	N/A	82.0±15.0	105.9±4.9
Mentor	1.5±0.04	N/A	N/A	56.3±7.0	42.7±5.5
Bost Sci midsection	0.58±0.15	4.0±0.9	20.1±3.4	37.7±4.0	48.4±6.2
Overall *P*	0.01	<0.001	<0.001	0.001	<0.001
Gynecare vs Bost Sci	0.3	0.9	0.9	0.95	>0.99
Gynecare vs AMS	>0.99	0.07	0.5	0.8	0.4
Gynecare vs Bard	0.08	< 0.001	< 0.001	0.1	0.005
Gynecare vs Caldera	<0.001	N/A	N/A	0.5	0.98
Gynecare vs Mentor	0.001	N/A	N/A	0.03	<0.001
Gynecare vs Boston Sci midsection	<0.001	<0.001	<0.001	<0.001	<0.001

The shape of the curves for Gynecare, Boston Scientific (Bost Sci) without its midsection, American Medical Systems (AMS), and Bard were nonlinear represented as an initial region of stiffness (low stiffness) and inflection point and a second region of increased stiffness (high stiffness) before failure. In contrast, the Caldera and Mentor meshes displayed a uniform linear behavior with a single stiffness throughout. The elongation relative to the initial length (relative elongation at failure, %) is also shown.

Overall *P* value from one way analysis of variance. Remaining *P* values represent pairwise comparisons between Gynecare and other brands made using Dunnett's multiple comparisons procedure.

[a] Mean and standard deviation of five independent slings

[b] Boston Scientific sling without midsection

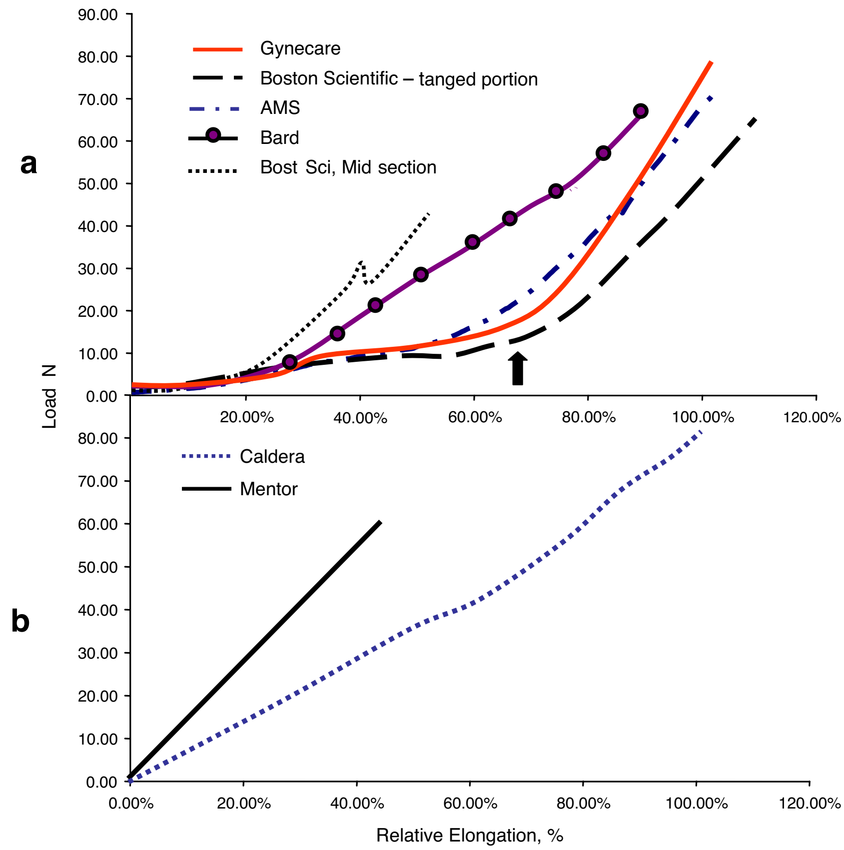

Fig. 3 Typical load relative elongation curves demonstrating nonlinear behavior for the Gynecare, Boston Scientific (tanged portion), AMS, Bard, and Boston Scientific midsection (**a**). The inflection point for the Gynecare sling, representing the transition between the regions of low stiffness (beginning portion of the curve with a flat slope) and the region of high stiffness (final steep portion of the curve with a steep slope), is shown with an *arrow*. In panel **b**, representative curves of the slings displaying linear behavior (Caldera and Mentor) with a single relatively high uniform slope are shown

remaining slings grossly appeared as a single linear piece of material. Thus, once these slings transitioned to the area of high stiffness, they had elongated to 40 to 50% greater than their original length. The Gynecare, the tanged non-heat-scaled portion of the Boston Scientific, and the AMS slings again demonstrated similar inflection point values measuring 2.0±0.3, 1.9±0.1, and 1.7±0.2 N/mm, respectively ($p>0.05$). The Bard samples and the Boston Scientific midsection were significantly different. The Bard samples demonstrated significantly lower values (1.2±0.1 N/mm, $p<0.05$), while the Boston Scientific midsection demonstrated the highest stiffness of any of the samples by a factor of 2 (4.0±0.9 N/mm, $p<0.05$). Interestingly, the AMS suture, tested separately, displayed linear behavior with a stiffness measuring 1.8±1.4 N/mm and rapid failure (elongation of 3–4 mm), indicating negligible contribution to the tensile properties of the AMS sling.

For the failure behavior, it should first be noted that nearly all samples failed at the clamp. Thus, these values likely underestimate the true failure values. Nevertheless, the smallest relative elongations at the point of failure were 42.7±5.5% (Mentor) and 48.4±6.2% (midsection of the Boston Scientific), with corresponding failure loads of 56.3±

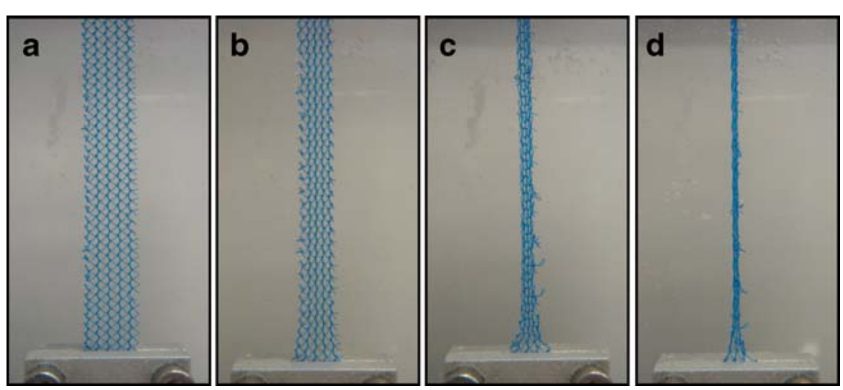

Fig. 4 Macroscopic images of a Gynecare sling at various stages of the tensile test: **a** preload, **b** low stiffness region, **c** the inflection point, **d** the high stiffness region. In the latter, the sling has elongated more than 70% of its original length and has lost its structural integrity such that it resembles a string

7.0 N and 42.7±5.5 N, respectively. Although this value (tensile strength) is the one most commonly reported by companies, they occur well beyond the elongations and forces that would be applied in vivo and are, therefore, not necessarily relevant to the clinical use of these slings. In this way, the behavior of the slings in the initial low stiffness region is likely most clinically relevant. For completeness, however, the results are as follows. The Gynecare, AMS, the tanged portion of the Boston Scientific, and Caldera samples showed similar values with relative elongations at failure ranging from 105.9± 4.9% (Caldera) to 115.2±7.4% (AMS) and loads at failure of ranging from 69.6±8.3 N (Boston Scientific) to 82.0±15.0 N (Caldera, $p>0.05$). The Bard mesh failed at a similar load to these slings (59.8±5.1 N); however, the relative elongation at failure was lower (92.3±6.7%, $p=0.005$). The Boston Scientific midsection had the lowest relative elongation and load at failure values (48.4±6.2% and 37.7±4.0 N, respectively; $p<0.001$), providing further evidence that heat sealing significantly increases the stiffness of this sling.

We developed a cyclical testing protocol to measure permanent elongation resulting from repetitive loading within a range of forces that are relevant for in vivo loading (cough, sneeze, straining, and moving from a sitting to standing position). After the completion of the cyclic loading protocol, none of the samples had failed. Typical curves for the Gynecare TVT™ are shown in Fig. 5, and the results for all samples are provided in Table 3. The permanent elongation after C1 (ten cycles between 0.5 and 5 N or roughly 0.1 and 1.1 lbs) of the Gynecare mesh was different from that of all the other samples tested. Gynecare samples permanently elongated by 17.5±4.2%, indicating that although very little force applied, there is irreversible deformation of the TVT™. The elongation value of the TVT™ was significantly higher but most similar to that of AMS (11.6±0.8%, $p=0.02$) and the tanged non-heat-sealed portion of Boston Scientific (11.9± 2.5%, $p=0.03$). Bard samples displayed significantly less permanent elongation after C1 (7.7±0.7%, $p<0.001$), while Caldera (2.5±1.0%, $p<0.001$) and Mentor (0.3±0.2%, $p<0.001$) showed very little permanent elongation with this cyclical protocol.

The permanent elongations after C2 (ten cycles between 0.5 and 15 N or roughly 0.1 and 3.4 lbs) were significantly greater for all samples ($p<0.001$). Relative to their initial length before C1, Gynecare samples permanently elongated 42.3±3.2%, which was similar to that of the AMS (43.4± 2.7%, $p>0.05$) and the tanged non-heat-scaled portion of the Boston Scientific sling (40.5±2.8%, $p>0.05$). Bard samples again displayed significantly less permanent elongation (26.2±3.4%, $p<0.001$), followed by Caldera (12.4±3.2%, $p<0.001$) and Mentor (3.4±0.2%, $p<0.001$). The lower permanent elongations indicate a much stiffer sling that is less likely than the TVT™ to deform when a load is applied. There were no significant changes in permanent elongation after C3, which consisted of repeating the protocol from C1 ($p>0.05$).

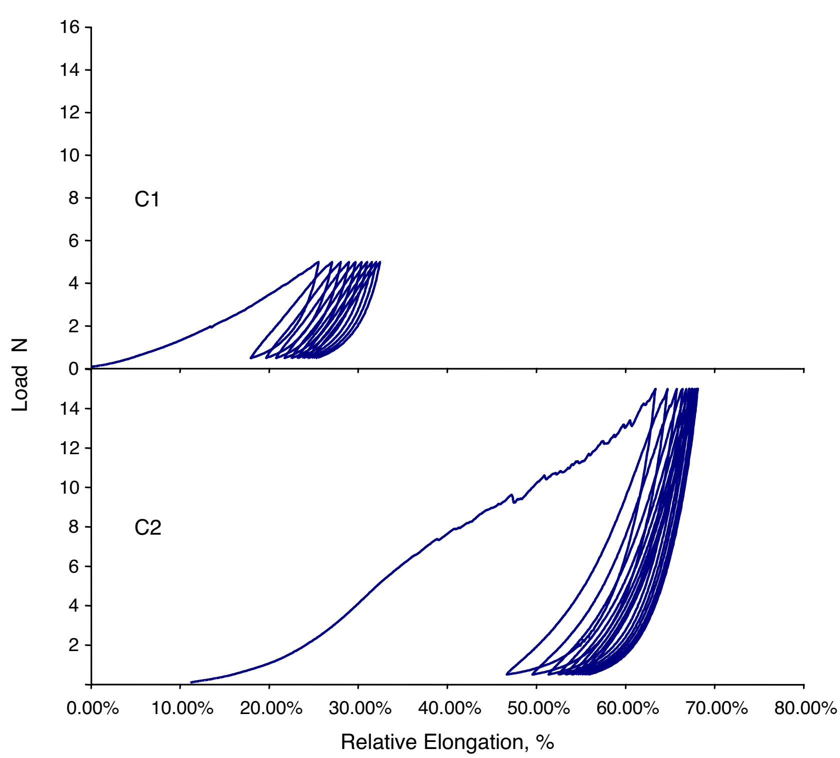

Fig. 5 Typical load elongation curves of the Gynecare sling after cyclical loading at C1 (ten cycles from 0.5 to 5 N) and C2 (ten cycles from 0.5 to 15 N). With each cycle, the peaks and valleys of the curve move pro gressively to the right of the graph indicating permanent (non reversible) elongation

Table 3 Cyclical loading test of the meshes listed in the leftmost column

Mesh	Permanent elongation after C1 (%)	Permanent elongation after C2 (%)
Gynecare	17.5±4.2[a]	42.3±3.2
Boston Scientific[b]	11.9±2.5	40.5±2.8
AMS	11.6±0.8	43.4±2.7
Bard	7.7±0.7	26.2±3.4
Caldera	2.5±1.0	12.4±3.2
Aris	0.3±0.2	3.4±0.2
Overall P^c	<0.001	<0.001
Gynecare vs Bost Scientific[b]	0.03	0.9
Gynecare vs AMS	0.02	0.98
Gynecare vs Bard	<0.001	<0.001
Gynecare vs Caldera	<0.001	<0.001
Gynecare vs Aris	<0.001	<0.001

In the first step (C1), samples were cycled between 0.5 and 5 N and the permanent elongation relative to the initial length was measured (%). In the second step (C2), the samples were cycled between 0.5 and 15 N, and the permanent elongation relative to the initial length was measured (%).

[a] Mean and standard deviation

[b] Boston Scientific sling without the midsection

[c] Overall *P* value from one way analysis of variance. Remaining *P* values represent pairwise comparisons between Gynecare and other brands made using Dunnett's multiple comparisons procedure.

Discussion

Stress urinary incontinence is a common and debilitating disease for women for which mid-urethral slings offer a relatively minimally invasive and effective approach to treatment [1]. Following the advent of the Gynecare TVT™, multiple manufacturers have developed their own version of the mid-urethral sling, all of which are widely used. All of the slings are wide-pore polypropylene mesh; however, each has been modified to improve on perceived deficiencies of the TVT™ purportedly without compromising efficacy. Although some of the biomechanical properties of the TVT™ and AMS Monarch have been described previously [7], little is known of how other newer products compare. In this paper, we maintain that before studying the impact of slings on tissue behavior in vivo and clinical outcome, physicians should have a good working knowledge of the textile and biomechanical properties of different slings ex vivo. This will arm clinicians with a common language when discussing the potential impact of slings on tissue behavior, clinical outcomes and will facilitate communication with biotechnology companies, features of a sling that may or may not be desirable. Therefore, in this study, we utilized two in-depth ex vivo mechanical testing protocols to better characterize and compare five commonly used polypropylene mid-urethral slings to the Gynecare TVT™.

The most important finding of the paper is that Gynecare TVT™ mesh has a unique tensile behavior which is characterized by an initial region of very low stiffness in which the mesh easily elongates in response to small changes in force. This is followed by a transition period (inflection point) and an area of high stiffness. As a result of this behavior, after cyclical loading at low loads (0.5 to 5 N or 0.1 to 1.1 lbs), Gynecare mesh permanently elongated by more than 10% of its initial length, confirming the easy permanent deformability of this mesh that is observed clinically during placement. The mesh with mechanical behavior most similar to Gynecare was that supplied by AMS.

With the exception of the tensioning suture in the AMS sling, the common endpoint of the modifications made by manufacturers to improve intraoperative handling of the mid-urethral sling was to increase stiffness. This makes intuitive sense, as stiffness describes the resistance of a material to increasing loads. Thus, these meshes were less likely to elongate under small loads (e.g., intraoperative manipulation or a small cough) and less likely to permanently deform with cyclical loading (e.g., a series of coughs). In contrast, the materials characterized by a very low stiffness such as the Gynecare and AMS meshes easily deformed under low loads. Clinically, this would manifest as elongation and deformation of the sling with the application of minimal tension. Importantly, elongation after cyclical loading was not reversible, indicating that once a sling deforms, it does not revert to its initial form.

At a glance, the behavior (low stiffness, easy deformability, and permanent elongation) of the Gynecare and AMS slings seems counterintuitive, as one could envision a hard cough or sneeze generating sufficient force to loosen the sling in the immediate or early postoperative period. However, such behavior in theory also lowers the rate of erosions of a sling into the urethra or bladder. In contrast, a high stiffness material may not yield (elongate) with the application of even high loads (a very heavy cough) and consequently would have an increased likelihood of erosion into the bladder or urethra. A low stiffness material may also make the sling less likely to obstruct the urethra or cause postoperative voiding dysfunction. Indeed, rates of these postoperative complications after the placement of a TVT™ mid-urethral sling may be less common than with traditional slings due to their biomechanical behavior [5, 6]. It will be interesting to determine whether postoperative complications are higher after the placement of a high stiffness sling. Although all of the slings examined in this study are widely used, there are currently no randomized trials comparing complication rates between a low stiffness and high stiffness sling.

Relative to the values provided by the companies on load at failure (Table 1), our values are similar or superior. Our values are also similar to those obtained for the Gynecare and AMS slings in a previous study [7]. Thus, in spite of observing failures at or near the clamps, these data suggest that our measured load at failure and relative elongations at failures are reasonable. While this provides a validation point for our data, it should be noted that previously published literature on the forces applied to mid-urethral slings in vivo is estimated to be in the range of approximately 5 to 15 N or 1.1 to 3.4 lbs [11]. Thus, if those estimates are accurate, the clinical relevance of load at failure and high stiffness is questionable, especially for the slings that demonstrated bilinear behavior (Gynecare, AMS, Boston Scientific without midsection, and Bard). At the point of failure, these slings had elongated 90–110% greater than their initial length. This degree of sling lengthening is not observed clinically, and therefore, not likely clinically relevant. Instead, the values found in this study for low stiffness, inflection point, and permanent elongation in response to cyclic loading may be more relevant to describe the function of these slings in vivo. Thus, we advocate that these measures should be supplied by the company instead of ultimate load at failure (often reported as tensile strength), as they are more likely to reflect the behavior of the sling in vivo in the perioperative and in the very early postoperative period.

Although it is important to understand the behavior of a sling before implantation, the behavior of these slings in vivo and after incorporation into host tissue may be inferred, but is not directly apparent from these studies. Indeed, the next logical step to the current study is the implementation of rigorous in vivo studies to determine how the textile and tensile properties of polypropylene slings relate to tissue behavior, efficacy, patient morbidity, and patient satisfaction. In the future, we also aim to use animal models to perform time-zero studies on the function of these implants in vivo and to explore their behavior after periods of healing and tissue incorporation. Ultimately, we hope to identify the parameters that are most relevant to efficacy and provide clinicians with quantitative data on sling selection with the goal of maximizing good patient outcomes.

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